Limitations of current indicators of micronutrient status

Lindsay H Allen

Assessment of micronutrient status is a major concern in public health nutrition, yet there are serious limitations to the indicators currently available. This paper presents the merits of these indicators along with their drawbacks, which include cost, lack of congruence between cutoffs denoting deficiency and adverse functional consequences, and inconsistent methods of evaluating the confounding effects of infections on micronutrient status indicators. Methods for assessing the functional consequences of micronutrient deficiencies are even less well developed; their usefulness would be enhanced by a greater focus on outcomes known to be influenced by deficiencies. Although there have been notable breakthroughs, further improvements in methods to assess micronutrient status are urgently needed.

INTRODUCTION

Assessment of the prevalence, causes, and consequences of micronutrient deficiencies has been a major focus of the public health nutrition community over the past two decades. There are still, however, considerable limitations to the available indicators of micronutrient status. The available indicators can be categorized as follows: measures of anemia and hematological status, including a complete blood count; levels of nutrients and metabolites in blood, urine, and breast milk; indicators of body stores, such as ferritin or the transferrin receptor:ferritin ratio for iron stores and the modified relative dose response (MRDR) test for liver retinol stores; and the prevalence of inadequate intake of each micronutrient, obtained by comparing intakes to the estimated average requirements (EARs).

USES OF MICRONUTRIENT STATUS INDICATORS

Research on the prevalence, causes, and consequences of micronutrient deficiencies, along with the monitoring and evaluation of the impact of interventions, often requires the most sophisticated methods of assessing micronutrient status. These are usually the most expensive and require the largest investment in equipment and personnel. Knowledge about the indicators of human functional responses to micronutrient status is still relatively limited. For example, to evaluate the effects of nutrition on infant or child development, methods are frequently used that have been validated by child development experts for other purposes but are not limited to or focused on specific developmental components known to be affected by micronutrient deficiencies. There is a lack of methods to assess many functions that may be altered by micronutrient status, although there has been progress in field methods for assessing a few functional outcomes, e.g., abnormal retinal function caused by vitamin A deficiency. Better techniques are needed urgently, and there is little doubt that these could be developed with the appropriate application of modern technology.

For larger-scale surveys and monitoring of interventions, it is usually important that the tests used to measure micronutrient status be feasible and affordable. Blood samples cannot usually be collected repeatedly from the same individual, and the volume required can be prohibitive, especially in infants and young children. There has been limited progress in the development of

Affiliations: *LH Allen* is with the United States Department of Agriculture, Agricultural Research Service, Western Human Nutrition Research Center, Davis, California, USA.

Correspondence: *LH Allen*, USDA, ARS Western Human Nutrition Research Center, 430 W. Health Sciences Drive, University of California, Davis, CA 95616, USA. E-mail: lindsay.allen@ars.usda.gov, Phone: +1-530-752-5268, Fax: +1-530-752-5271.

field-friendly, affordable instrumentation, such as the Hemocue for hemoglobin analysis and the portable hematofluorometer for determining zinc protoporphyrin levels. Many biochemical tests can be performed for US$1–US$3 per assay, but others are still too expensive for large-scale surveys, e.g., the transferrin receptor test and the methylmalonic acid test. The equipment required for some important assays is also too costly for many laboratories, such as atomic absorption spectrometers for zinc analyses or high-pressure liquid chromatographs for retinol and riboflavin assessment. With many assays, the handling and storage of samples remains a challenge, although there have been advances in techniques to dry serum or blood samples on filter paper for later assessment of retinol, ferritin, and other indicators of micronutrient status. One notable breakthrough in this regard is the application of a sandwich ELISA assay for measurement of ferritin, transferrin receptors, retinol-binding protein, and C-reactive protein (CRP) in dried blood spots.[1]

Cutoff values have been established for most indicators, denoting whether status is deficient, marginal, or adequate. However, these are not usually the cutoffs that would clearly indicate the risk of a public health problem. For example, it is not clear that there are functional abnormalities in individuals whose serum vitamin B_{12} concentration is <150 pmol/L, or whose erythrocyte glutathione reductase coefficient is between 1.2 and 1.4. Furthermore, a positive response of status indicators to an intervention does not mean that health or function has been improved, and a lack of response can still be accompanied by improved health or developmental outcomes.

Assessment of the effect of current infections on micronutrient status indicators is lacking in uniformity and thus presents a serious problem. For example, the acute-phase response to infection affects indicators of retinol, iron, and zinc status. The application of acute-phase response indicators, such CRP or alpha 1-acid glycoprotein (AGP), tends to be inconsistent, and consensus is needed on which indicators to use in specific situations, when they must be used, and how to use them in data analysis and interpretation. Malaria is the most common cause of severe anemia and can confound the interpretation of most iron status indicators; in malaria, ferritin and transferrin receptor concentrations are often elevated, while CRP and AGP concentrations are not always affected. The recent World Health Organization (WHO) recommendation that iron supplementation in areas of endemic malaria should be targeted only to iron-deficient children[2] creates new urgency for the development of methods and equipment that make it feasible to measure iron status in such children on a large scale and at minimal cost.

MICRONUTRIENT STATUS INDICATORS FOR GUIDING FORTIFICATION PROGRAMS

In order to estimate the type and amount of micronutrients to add to staples in fortification programs, it is recommended that 2 days of usual food intake data be collected from approximately 100 people in each population group of concern, e.g., poor women of childbearing age, young children, or groups with specific food preferences and avoidances for religious or cultural reasons.[3] Based on micronutrient intakes calculated from the food intake data, the difference (gap) between these intakes and the recommended intakes (EARs) for each nutrient can be calculated in each population group. In addition, the intake data can be used to estimate the usual distribution of intake of foods that are under consideration for fortification. The final step is then to simulate the effect of different levels of fortification on the prevalence of inadequate intake of each micronutrient, for each population group of concern. Ideally, improvements are needed in the following areas: knowledge of the micronutrient content in local foods as well as the bioavailability of such micronutrients; an updated database on international food composition; and availability of a software package (currently being developed) to enable estimation of the amount of micronutrient fortificants to add to staples based on the above procedures.

To monitor the effectiveness of programs, it would be helpful to have good indicators of the effect of fortification on body stores of a nutrient. An example of an ideal measure for this purpose is the ratio of transferrin receptors to ferritin, from which body iron can be calculated. The development of this indicator has made it feasible to test the effect of fortification strategies on changes in body iron stores and on bioavailability of the fortificant iron (e.g., amount consumed/increase in body iron stores).[4] Ways to estimate change in body stores are still needed for the majority of micronutrients.

ESTIMATING THE ADEQUACY OF MICRONUTRIENTS IN DIETS

Most individuals in poorer populations in underdeveloped countries suffer from a number of micronutrient deficiencies simultaneously (usually vitamin A, iron, riboflavin, vitamin B_{12}, and zinc, due to a low intake of foods from animal sources). Examples of indicators of the overall adequacy of micronutrients in diets include the mean probability of inadequate intake (intake <EAR) for a number of micronutrients,[5] dietary diversity scores, and the amount of specific micronutrient-rich foods consumed (e.g., percent energy consumed as foods from animal sources).

Calculation of the probability of inadequate intake for each micronutrient is a relatively recent approach.[6] An inadequate intake is defined as one that does not meet the EAR. Unfortunately, many countries still publish only recommended dietary intakes and not EARs. Recommendations of the Food and Agricultural Organization and the World Health Organization for nutrient intake do not include EARs, although these have been estimated for the purpose of determining appropriate micronutrient additions in fortification programs.[3]

CONCLUSION

Compared to the technological advances that have been made in most areas of science, assessment of the prevalence and consequences of micronutrient deficiencies is still at a relatively primitive stage of development. The result is widespread ignorance of the prevalence of most micronutrient deficiencies and their functional consequences. Subsequently, most investment in interventions to improve status is limited to a few micronutrients. The global databases of the World Health Organization, for example, contain information only on the prevalence of anemia (but not the prevalence of iron deficiency or iron-deficiency anemia) and on iodine, vitamin A, folate, and vitamin B_{12} deficiencies, and for some of these micronutrients the data are sparse. Investment in the development of new methods to assess micronutrient status should receive high priority.

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